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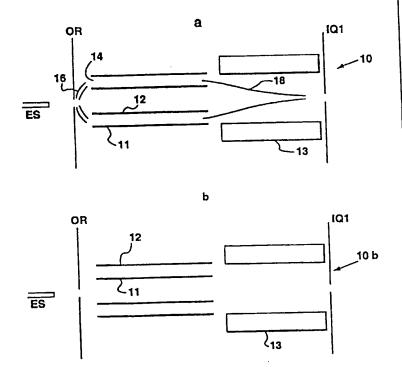
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(54) Title: MASS SPECTROMETER, INCLUDING COUPLING OF AN ATMOSPHERIC PRESSURE ION SOURCE TO A LOW PRESSURE MASS ANALYZER

(57) Abstract

(30) Priority Data:

A method of transporting ions from a region at a relatively high pressure to a region at a relatively low pressure comprises generating ions in a first region at a relatively high pressure, for example at atmospheric pressure. The ions are then passed from the first region into a second region containing a device comprising a pair of spaced apart electrodes, preferably a pair of cylinders, the second region being maintained at a relatively low pressure. An asymmetric RF voltage and a DC compensating voltage are applied to the electrodes, whereby ions of interest follow a stable trajectory through the electrodes, and the ions pass out of the space between the electrodes in the second region. Gas is displaced or pumped from the second region to maintain the second region at the relatively low pressure. The ions pass out of the second region into a third region maintained at a lower pressure than the first and second regions. A corresponding apparatus is provided.



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Title: MASS SPECTROMETER, INCLUDING COUPLING OF AN ATMOSPHERIC PRESSURE ION SOURCE TO A LOW PRESSURE MASS ANALYZER

FIELD OF THE INVENTION

This invention relates to mass spectrometry, and more particularly is concerned with the coupling of an atmospheric pressure ion source to a mass analyzer operating at a very low pressure.

BACKGROUND OF THE INVENTION

Since the discovery of atmospheric pressure ionization, electrospray ionization-mass spectroscopy, ESI-MS, has proven to be a sensitive analytical tool in many fields of science. One of the most challenging efforts has been and continues to be the introduction of a high yield of ions formed by ESI source, into the mass analyzer. Most mass analyzers function at relatively low pressure of, for example 1 x 10⁻⁵ torr. The most common and practical way to introduce ions into the mass analyzer is by directing ions through a number of intermediate differentially pumped regions. A disadvantage of this process is that only a few percentage of ions can be introduced into the mass analyzer.

Because of the high pressure differences between the different regions, to maintain these pressure differences dividing walls or partitions are provided. To enable ions to pass through, slits or holes are provided, but these are small, to keep pumping requirements and gas flow rates reasonable, and hence many ions do not find their way through the slits and/or holes and are lost.

As mass spectrometry is becoming a common analytical tool, new demands to improve and enhance the technique, to make it more applicable to other analyzing fields, are required. Since the useful applications of this technique are defined by overall sensitivity and, despite many advances in recent years, there is still a great interest in developing new approaches to enhance the sensitivity of this technique.

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The recent development of high Field Asymmetric Ion Mobility Spectroscopy (FAIMS) provides a device in which a high yield of ions can be transported in the annular space between two coaxial cylinders. In this technique, ions are subjected to an asymmetric wave form in a range of radio frequencies, RF, at atmospheric pressure and at room temperature. Fundamentally, this technique relies upon the discovery that ion mobility can vary with the applied field, and moreover, different ions exhibit different variations in mobility. Then, application of a highly asymmetric RF field causes different ions to migrate in different directions. By selection of a suitable compensating DC voltage, the migration of a desired ion can be balanced, so that this ion will maintain a steady path between the pair of cylinders or plates applying the field. Other ions, with different migration characteristics have unstable ion trajectories, and these ions tend to diverge and collide with one or other of the tubular plates.

Now, the ion mobility depends upon the ratio of applied electric field to number density, i.e. E/N. When applied at atmospheric pressure, FAIMS requires a high asymmetric RF voltage, of the order of 2,000 to 5,000 volts, at a frequency of 100-200 kHz.

Now, many present ESI-MS instruments commonly have a number of differential pumped regions, at successively lower pressures, and these are found in the API 2000 and API 3000 spectrometers designed by the MDS-Sciex division of Concord, Ontario, the assignee of the present invention. For example, in such spectrometers for analyzing organic products, ions are introduced into the first differentially pumped interface region through a 250 µm sampling orifice. This interface region, with appropriate pumping, is normally kept at 1-2 torr pressure. Ions are then sampled from the free jet expansion in this region through a skimmer and are directed to a second differentially pumped region maintained at a lower pressure and containing a first rod set (not shown). The skimmer has an orifice with a diameter of 0.5 to 3 mm. As mentioned, this results in low ion transmission efficiency.

FAIMS has been interfaced to a mass spectrometer at

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atmospheric pressure through a 250 µm orifice at the end of the outer coaxial cylinder. Since ions are distributed in the annular space between the cylinders, to give a toroidal cloud of ions, only a small portion of the ions are effectively sampled. This in turn reduces the sensitivity of the mass spectrometer. Unfortunately, there is no simple way available, in the atmospheric pressure region, to overcome effectively the dispersion of the ion cloud as a result of Coulombic repulsion or to reverse the effects with gas dynamics.

The present inventors have now realized that the FAIMS technique can be readily applied to the interface region of a mass spectrometer, and can offer a number of advantages. Because of the geometry of the cylinders of a FAIMS device, it could be coupled to an electrospray source with little modification. It should enable a high yield of ions to be injected into the annular space between the tubes. Ions can be introduced into this annular space directly from the free jet expansion (less than 10 mm from the sampling orifice) or alternatively, at a distance further away and outside the free jet expansion region.

At atmospheric pressure, the RF frequency and amplitude are limited because of the high power requirements. However, at a lower pressure region it is expected that the RF level reduces according to the E/N (Electric Field to Number Density) ratio. The application of lower RF power makes it possible to optimize the physical geometry and RF frequency of the coaxial tubes for better efficiency and greater separation of ionic species. Additionally, since the FAIMS device operates at a lower pressure, this enables a number of different techniques to be applied to extract most, if not all, of the ions that have been introduced in the coaxial tubes. Examples of these are: ion guides, quadrupole rods, quadrupole rods with axial field components, and electrostatic lenses. Also, gas dynamics can be better and more effectively utilized, to control the ions and ensure a high yield of ions.

Additionally, the separation and focusing capability of FAIMS has the great consequence of advancing the overall sensitivity of the ESI-MS. Firstly, the filtering ability of FAIMS can significantly reduce the

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inherent background noise which is attributed to large clusters of ions that carry a large number of charges. Secondly, RF field confinement reduces the ion scattering loss and benefits from collisional focusing phenomena. Collisional focusing in a quadrupole is described in U.S. patent 4,963,736.

There are a number of other potential gains that should be realized with the use of the FAIMS interface. One can have an effectively much increased orifice size, yielding a higher flux of ions. The FAIMS device can be applied over a large pressure range from 0.1 to 100 Torr, allowing for other applications than those discussed. As noted, at lower 10 pressures, the overall geometry of the coaxial tubes requires lower voltage requirements, which in turn eliminates the requirement for a high voltage RF generator, which can be complex and expensive.

SUMMARY OF THE INVENTION

In accordance with the present invention, there is provided a method of transporting ions from a region at a relatively high pressure to 15 a region at a relatively low pressure, the method comprising:

- passing ions from a first region at relatively high pressure into a second region containing a device comprising a pair of spaced apart electrodes, the second region being maintained at a relatively low pressure;
- applying an asymmetric field and a DC compensating (2) field to the electrodes, whereby ions of interest follow a stable trajectory through the electrodes;
- passing the ions out of the space between the (3) 25 electrodes in the second region;
 - displacing gas from the second region to maintain the second region at the relatively low pressure; and
 - passing the ions out of the second region into a third region maintained at a lower pressure than the first and second regions.
- 30 Conveniently, the ions are generated at atmospheric pressure in the first region.

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Preferably, the method includes maintaining the second region at a pressure in the range of 0.1 - 100 Torr, and the third region at a pressure in the range of 2-12 mTorr.

Preferably, the electrodes are provided as a pair of coaxially spaced cylinders. Then, the ions can be passed out of the annular space between the cylinders into one of: a quadrupole rod set; a ring guide; and an array of electrostatic lenses.

Another aspect of the present invention provides an apparatus, for transporting ions from a region at a relatively high pressure to a region at a relatively low pressure, the apparatus comprising:

an inlet for ions from the first region at relatively high pressure;

a pair of spaced apart electrodes defining a space for ion transport;

a device for collecting and focussing ions exiting the spaced apart electrodes;

an outlet adjacent the collecting and focussing device for receiving ions and passing ions through to a lower pressure region, wherein the spaced apart electrodes and the device for collecting and focussing are located in a chamber between the inlet and the outlet.

Conveniently, the apparatus includes: an atmospheric ion source located in a first region, and an orifice connecting the ion source to the chamber, the chamber defining a second region housing the spaced apart electrodes and the device for collecting and focussing.

Preferably, the device for collecting and focussing comprises one of a quadrupole rod set, a ring guide and an array of electrostatic lenses, mounted to receive ions from the spaced apart electrodes.

BRIEF DESCRIPTION OF THE DRAWINGS

For a better understanding of the present invention and to show more clearly how it may be carried into effect, reference will now be

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made, by way of example, to the accompanying drawings which show the preferred embodiments of the present invention and in which:

Figure 1a is a schematic view of a first embodiment of an apparatus in accordance with the present invention;

Figure 1b is a schematic view of the apparatus of Figure 1a showing a variant thereof;

Figures 2 and 3 show schematic views of second and third embodiments of an apparatus in accordance with the present invention;

Figures 4a and 4b show a fourth embodiment of an apparatus in accordance with the present invention, and a variant thereof; 10

Figures 5-9 show five further embodiments of the present invention.

DESCRIPTION OF THE PREFERRED EMBODIMENTS

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Referring first to Figure 1, the first embodiment of the apparatus is indicated generally by reference 10. This apparatus 10 has an 15 electrospray source ES discharging towards an orifice in a plate indicated at OR, in known manner. The orifice in plate OR has a diameter in the range from 0.1 to 2.0 mm. At the other end of the apparatus there is an interquad aperture indicated at IQ1, provided with an aperture in its middle, in 20 known manner and with a diameter in the range from 1.0 to 3.0 mm. These components are common to many mass spectrometer designs, and also are found in many of the other embodiments of the invention. For simplicity and brevity, the description of these components will not be repeated.

In this first embodiment 10, there is a pair of tubes or 25 cylinders indicated at 11, 12, coaxially mounted with respect to one another. These tubes 11, 12 would be coupled to a suitable RF source, for applying a radial RF field between them. Additionally, the voltage source would be capable of providing a compensating DC voltage between them, to enable the FAIMS technique to be applied to them. Further details of the FAIMS technique can be found in U.S. patent 5,420,424 (Mine Safety Appliances). 30 Appropriate voltages would be selected so that ions with a desired mobility

would be stable and would pass through the cylinders 11, 12.

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Thus, the tubes 11, 12 provide an input annulus indicated at 14, for receiving ions from the orifice OR. The ion flow is indicated schematically at 16. It will appreciated that this configuration will not necessarily capture all the ions coming through the orifice OR.

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Upon exiting the annulus between the cylinders 11, 12, the ions pass into a first quadrupole rod set 13. This operates as a collisional focusing rod set. It is collisional in the sense that a relatively high pressure is present. It is anticipated that the pressure in the interface region between the orifice OR and the interquad aperture IQ1 would be in the range 0.1-100 torr. Consequently, the rod set 13 will operate in a collisional mode.

The rod set 13 also operates to focus the ions towards the central axis. Ion flow is indicated schematically at 18. Thus, ions will leave the annulus between the cylinders 11, 12 and track towards the central axis, for passage through the interquad aperture IQ1.

Figure 1b shows the same arrangement as Figure 1a. Here, an axial field is provided along the quadrupole rod set 13. Otherwise, the components in Figure 1b are the same as in Figure 1a, and the overall apparatus is indicated at 10b.

To provide the axial field, resistive rods could be provided, as detailed in U.S. patent 5,847,386, the contents of which are hereby incorporated by reference. The resistive rods establish a DC potential that drops uniformly along the length of the rods. Alternatively, the rods could be segmented into a number of short sections, with each section maintained 25 at a different DC potential, again to provide the necessary desired axial field, so as to drive the ions towards the interquad aperture IQ1.

Reference will now be made to Figure 2, which shows a second embodiment in the apparatus indicated generally by the reference 20. Again, the pair of cylinders or tubes 11, 12 and the source ES are 30 incorporated. Here, the ions discharge from the cylinders 11, 12 into a ring guide indicated at 22. The ions on exiting the cylinders 11, 12 flow through the ring guide 22, as indicated at 24. The ring guide 22 comprises a stack of

parallel spaced apart plates. These plates have circular apertures 26 which vary in diameter, so that the ion beam reduces in diameter towards the interquad aperture IQ1. This ring guide is in accordance with a design developed by Richard Smith of Batelle Northwestern Laboratories, Washington State, U.S.A., as disclosed in more detail in a paper entitled "An Ion Funnel Interface for Improved Ion Focusing and Sensitivity Using Electrospray Ionization Mass Spectrometry" by Scott A. Shaffer et al, (Analytical Chemistry, Vol. 70, No. 19, October 1, 1998, 4111-4119), the contents of which are also hereby incorporated by reference. In known manner, every other element or lens of the ring guide 22 is connected to one side of a power supply (providing RF and/or DC voltages) and the alternate, interleaning elements are connected to the other side of the power supply.

A third embodiment is shown in Figure 3. Here, ions from the annulus between the cylinders 11, 12 discharge into a zone between a series of electrostatic focusing lenses 32. The electrostatic lenses 32 present a series of apertures 34 which focus ions through the interquad aperture IQ1. The motion of the ions is indicated at 36.

A fourth embodiment is shown in Figures 4a and 4b, with the two variants being indicated at 40a and 40b. Again, the ES source is provided and the cylinders are indicated at 41, 42. Here, the interquad aperture IQ1 is positioned perpendicularly to the orifice OR. The cylinders of the FAIMS device are here modified and are indicated at 41 and 42. The inner cylinder 42 is a plain cylinder while the cylinder 41 includes an exit opening 44. Again, the device is intended to operate in the pressure region of 0.1-100 torr.

The quadrupole rod set is here indicated at 46 and is aligned with its axis centered on the opening 44 and with the interquad aperture IQ1.

This embodiment is intended to function in the same manner as that of Figures 1a, 1b. Accordingly, Figure 4b shows a modification with a rod set, here indicated at 48, adapted to provide an axial

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DC field. As for Figure 1b, this can be achieved by either providing additional resistive rods as detailed in U.S. patent 5,847,386.

Figures 5 and 6 shows fifth and sixth embodiments, which are orthogonal versions of the second and third embodiments of Figures 2 and 3, in the same manner that the fourth embodiment is an orthogonal version of the first embodiment. The cylinders forming the FAIMS device are indicated at 41, 42, as in Figure 4. The aperture is again indicated at 44, but in these fifth and sixth embodiments, the aperture 44 can be sized according to the characteristics of the focusing device.

Thus, in Figure 5, a ring guide is provided, indicated at 52. This ring guide can be comparable to the ring guide 22, and again in accordance with the paper by Scott A. Shaffer et al, detailed above.

Similarly, in the sixth embodiment indicated at 60 in Figure 6, electrostatic lenses 62 are provided. The lenses 62 similarly can be configured as the lenses 32 of Figure 3.

Reference will now be made to Figures 7 and 8, which show alternate variations of the basic FAIMS unit. These are intended to provide configurations which will improve collection of ions from the electrospray source, and simultaneously eliminate the necessity for any focusing device immediately upstream from the interquad aperture IQ1.

Referring first to Figure 7, the seventh embodiment is indicated generally at 70. Here, the FAIMS device is configured with an outer tube or cylinder 71, which abuts against the orifice plate OR; it would however be electrically insulated from the orifice plate OR. Internally, there is a cylinder 72 provided with hemispherical end portions 73 and 74.

The hemispherical end 73 would be spaced from the orifice in the orifice plate OR, so that the cone of ions admitted through the orifice OR are all substantially captured in the annular gap indicated at 75.

Adjacent to the interquad aperture IQ1, the outer cylinder
30 71 terminates short of the interquad aperture IQ1, to leave an annular space
76. This enables gas and solvent vapour to exit as indicated by the arrows.
As with the other versions, the region outside of the cylinder 71 would be

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pumped down to the pressure in the range 0.1-100 torr.

The hemispherical end 74 is spaced from the interquad aperture IQ1 so that there is a high efficiency of ions passing through the interquad aperture IQ1 into the mass analyzer on the other side thereof.

Referring to Figure 8, there is shown an eighth embodiment indicated generally by the reference 80. This embodiment 80 has the FAIMS device configured with an outer cylinder 81, and the inner cylinder provided just by a wire or rod 82. In effect, the cylindrical outer surface of the wire 82 provides the inner cylinder. This eliminates the problem of an inner cylindrical space into which ions can pass and in which the ions will not be focused by the FAIMS effect, but rather will be lost. Here, the outer cylinder 81 is shown spaced from the orifice OR, but as for the seventh embodiment, it could abut the orifice OR. Again, an annular space, indicated here at 83 is provided between the cylinder 81 and the interquad aperture IQ1, for gas insolvent vapour to be vented.

As indicated schematically at 84, the provisions of the simple wire 82 should enable a high percentage of the ions to be captured within the annulus between the wire 82 and cylinder 81.

The ends of the wire 82 can be positioned or adjusted so as to give high efficiency for capture of ions at the inlet, and to permit ions to pass sufficiently through the aperture or orifice in the interquad aperture IQ1.

Reference will now be made to Figure 9, which shows a tenth embodiment indicated generally by the reference 100. Here, two FAIMS devices are provided, one comprising a pair of cylinders 101, 102 and the other comprising a pair of cylinders 103, 104. As shown, pairs of cylinders can have generally similar dimensions, although this is not necessarily essential. At the inlet to the pair of cylinders 101, 102, there is an electrospray source indicated at 106. Between the two pairs of cylinders, there is an orifice plate 108 provided with an annular orifice 110.

The intention here is that ions from the electrospray source 106 will be caught and focused between the pair of cylinders 101, 102. The

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electrospray source 106 and the cylinders 101, 102 are all at atmospheric pressure.

Ions would then pass through the annular orifice 110 into another chamber maintained at a pressure in the range of 1-10 torr. The ions would then continue to be focused by the cylinders 103, 104. The ions then pass through an interquad aperture (not shown here, but as in earlier figures), to the first stage of a mass analyzer.

The voltages applied to the cylinder pairs 101, 102 and 103, 104 would be such as to capture the same ions. Because of the different pressure regimes, this would require different voltages. Nonetheless, the two FAIMS devices can be adjusted to capture or focus the same ions.

This arrangement is expected to provide efficient coupling between an atmospheric source and a mass analyzer operating at a low pressure of, for example, 10-5 torr. As for all FAIMS devices, ions are focused radially by the applied fields, and ion motion axially is achieved by gas dynamics, i.e. the gas flow through the device.

A further option applicable to all the embodiments of the present invention is to provide the outer cylinder at least as a porous or mesh cylinder. Then it can still provide the necessary electric fields, but it enables gas to pass through the mesh. This might provide more controlled venting of gas removed between the orifice plate OR and the interquad aperture plate IQ1, and hence prevent occurrence of excessive gas velocities at any point that might tend to deflect ion flow.

CLAIMS:

- 1. A method of transporting ions from a region at a relatively high pressure to a region at a relatively low pressure, the method comprising:
- 5 (1) passing ions from a first region at relatively high pressure into a second region containing a device comprising a pair of spaced apart electrodes, the second region being maintained at a relatively low pressure;
- (2) applying an asymmetric field and a DC 10 compensating field to the electrodes, whereby ions of interest follow a stable trajectory through the electrodes;
 - (3) passing the ions out of the space between the electrodes in the second region;
- (4) displacing gas from the second region to maintain 15 the second region at the relatively low pressure; and
 - (5) passing the ions out of the second region into a third region maintained at a lower pressure than the first and second regions.
- 2. A method as claimed in Claim 1 which includes 20 generating ions at atmospheric pressure in the first region.
 - 3. A method as claimed in Claim 2, which includes maintaining the second region at a pressure in the range of 0.1 100 Torr.
 - 4. A method as claimed in Claim 3, which includes maintaining the third region at a pressure in the range of 2 to 12.0 mTorr.
- 25 5. A method as claimed in Claim 3, which includes providing the electrodes as a pair of coaxially spaced cylinders.

- 6. A method as claimed in Claim 6, which includes passing the ions out of the annular space between the cylinders into one of: a quadrupole rod set; a ring guide; and an array of electrostatic focusing lenses.
- 5 7. An apparatus, for transporting ions from a region at a relatively high pressure to a region at a relatively low pressure, the apparatus comprising:

an inlet for ions from the first region at relatively high pressure;

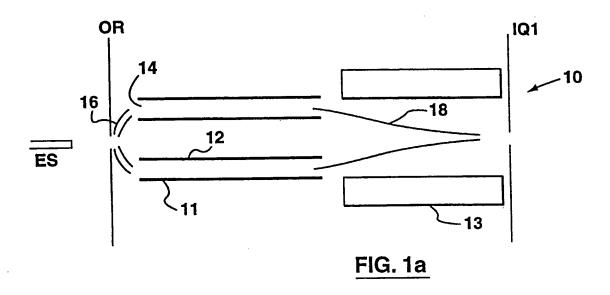
a pair of spaced apart electrodes defining a space for ion transport;

a device for collecting and focussing ions exiting the spaced apart electrodes;

an outlet adjacent the collecting and focussing device for receiving ions and passing ions through to a lower pressure region, wherein the spaced apart electrodes and the device for collecting and focussing are located in a chamber between the inlet and the outlet.

- 8. An apparatus as claimed in Claim 8, which includes: an atmospheric ion source located in a first region, and an orifice connecting the ion source to the chamber, the chamber defining a second region housing the spaced apart electrodes and the device for collecting and focussing.
 - 9. An apparatus as claimed in Claim 9, wherein the electrodes comprise a pair of spaced apart cylinders.
- 25 10. An apparatus as claimed in Claim 10, wherein the device for collecting and focussing comprises one of a quadrupole rod set, a ring guide and an array of electrostatic lenses, mounted to receive ions from the spaced apart electrodes.

11. An apparatus as claimed in Claim 9, wherein the ion source comprises an electrospray source, and wherein an additional aperture is provided separating the chamber from a further chamber defining a third region containing mass analyzer devices.



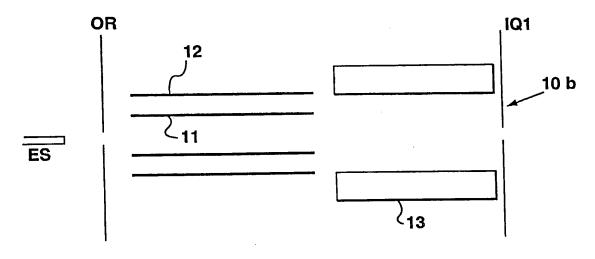


FIG. 1b

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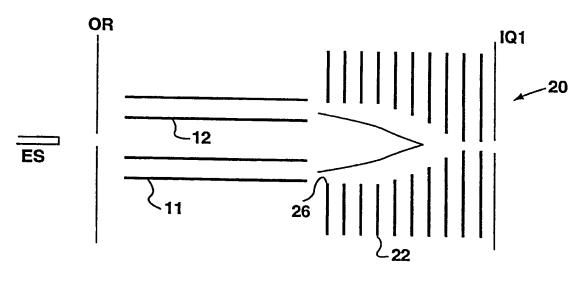
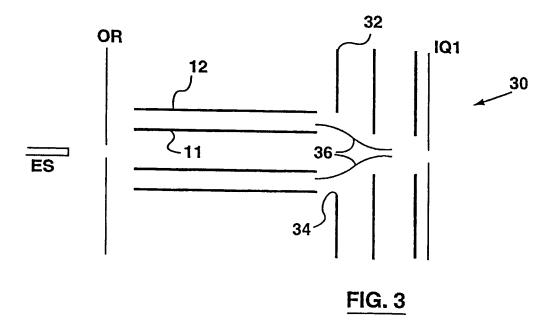
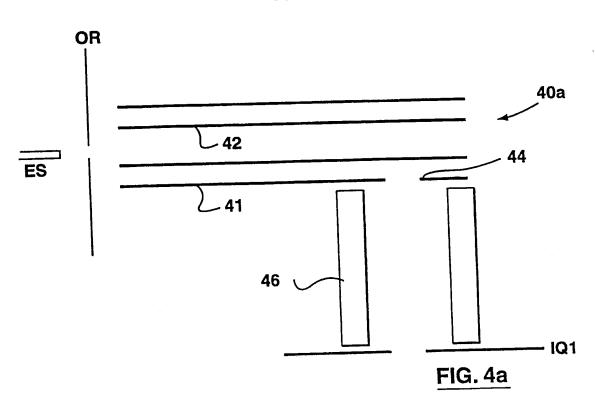
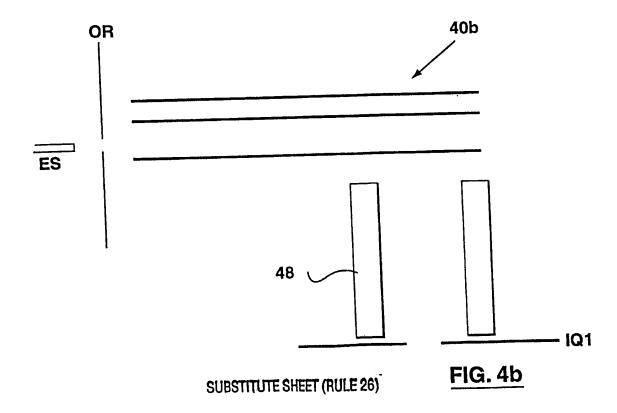


FIG. 2



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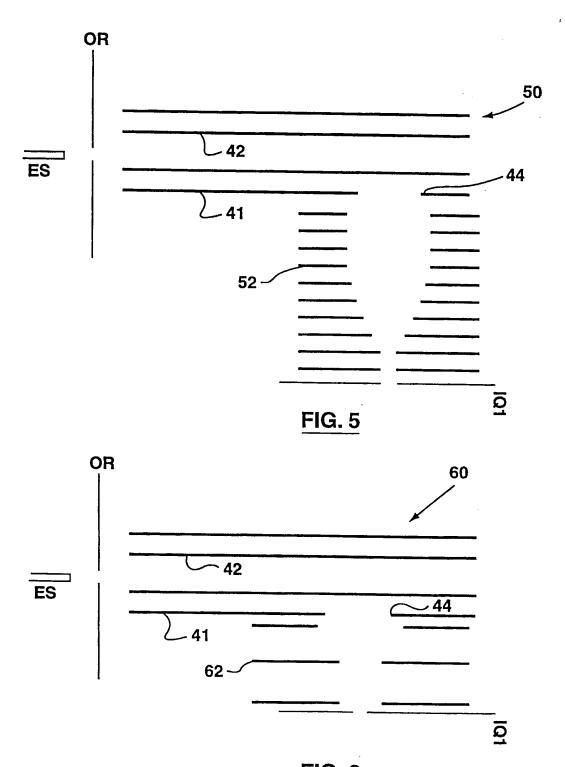


FIG. 6

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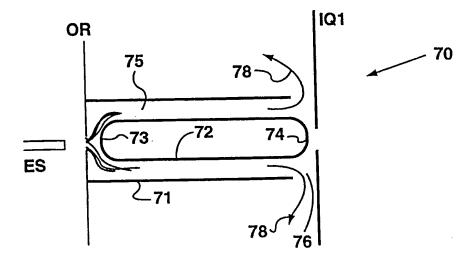
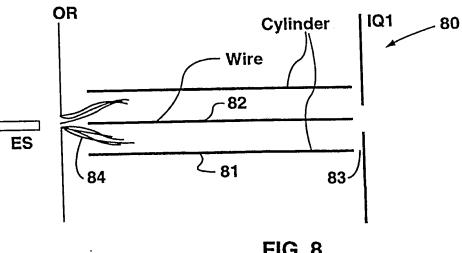


FIG. 7



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FIG. 8

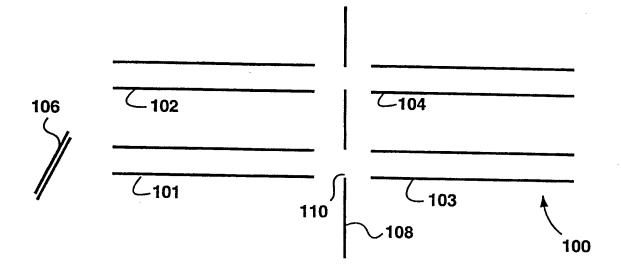


FIG. 9

INTERNATIONAL SEARCH REPORT

Intel onal Application No PCT/CA 00/00416

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	page 21, line 11,12 claims 1,3-5,7 figures 3,5	·	
X Fu	urther documents are listed in the continuation of box C.	Patent family members are	listed in annex.
.V. qoon	ment defining the general state of the art which is not widered to be of particular relevance	"I" later document published after to or priority date and not in confi- cited to understand the principl invention "X" document of particular relevance	e or theory underlying the
"L" docu whi cits "O" doc oth	er document but published on or after the international og date ment which may throw doubts on priority claim(s) or ich is died to establish the publication date of another tition or other special reason (as specified) ument referring to an oral disclosure, use, exhibition or ier means ument published prior to the international filing date but er than the priority date claimed	cannot be considered novel or involve an inventive step when "Y" document of particular relevance cannot be considered to involve document is combined with or ments, such combination bein in the art. *&* document member of the same	the document is taken alone te; the claimed invention re an inventive step when the te or more other such docu- g obvious to a person skilled
•	the actual completion of the international search	Date of mailing of the internation 21/08/2000	onal search report
Name s	11 August 2000 and mailing address of the ISA	Authorized officer	

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Winkelman, A

INTERNATIONAL SEARCH REPORT

Inter onal Application No PCT/CA 00/00416

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		PCT/CA 00/00416		
Category *	Citation of document, with indication, where appropriate, of the relevant passages			
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